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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,416	11/28/2000	Hong Jin	7682-052-999	7604

20583 7590 01/20/2004

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,416	JIN ET AL.	
	Examin r	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover she t with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10-23-2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after a Final rejection (mailed on February 25, 2003). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on July 25, 2003 have been entered.

2. In the RCE, previously pending claims 1-48 were cancelled from the application, and new claims 49-53 were added. Claims 49-53 are now pending and under consideration to the extent that they read on the elected inventions.

Inventorship

3. In view of the papers filed October 23, 2003, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by adding to the list of inventors David Kirkwood Clarke, and Peter M. Palese.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Priority

4. As indicated above, the Applicant has corrected the inventorship of the present application such that it now shares commonly named inventors with prior applications 09/161,122, and 08/316,439. Thus, the Applicant has complied with the requirements of 35 U.S.C. § 120for a claim for priority to the earlier applications.

5. **(New objection)** The specification is objected to because the reference in the specification to the priority document should indicate the relationship between the applications. See, 37 CFR 1.78(a)(2)(i). In specific, the reference does not indicate whether the 09/161,122 application is a CIP, a continuation, or a divisional of the 08/316,439 application, and thus does not fully identify the relationship between the 08/316,439 application and the present application.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on October 23, 2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. It is noted that this IDS is identical to that submitted on July 25, 2003. In view of this, the July 2003 IDS has not been considered separately by the Examiner.

7. It is noted that Reference CQ of the October 2003 IDS has been crossed out on the reference listing. This reference was previously made of record and considered in the IDS of March 2001.

Specification

8. **(Prior Objection- Withdrawn)** The amendment filed December 5, 2002 was objected to in the Final action under 35 U.S.C. 132 because it introduces new matter into the disclosure. The added material, which was not supported by the original disclosure, was the incorporation by reference of the material of prior application 08/316,439. In view of the amendment of the Application to cancel the New Matter, the objection is withdrawn.

9. **(New Objection)** The specification is objected because it appears to lack proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). In specific, although there is written description support in the application for the claim language requiring the presence of "an mRNA coding sequence operatively linked to a polymerase binding site of' RSV in originally filed claim 17, there does not appear to be antecedent basis support for that claim language in the specification of the present application. Applicant is required either to point out where such antecedent basis support lies in the specification, or to amend the application to correct the oversight.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. **(New Rejection)** Claims 51-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on attenuated RSV virus with genetic alterations in a key regulatory or functional domain. However, the application does not define what is meant by a key regulatory or functional domain, and there are multiple possible interpretations of the language. First, it is unclear if the key functional or regulatory domains refer to the key functional or regulatory domains of any RSV gene, or if they refer only to the regulatory or functional domains of key genes of the RSV genome. I.e., it is not clear if the term "key" refers to the domain's importance to a particular gene or to the virus as a whole.

Further, if, by referring to "key" domains, the claims are referring to key genes of the viral genome, it is further unclear what genes are included by this description. For example, the art recognizes that the minimum genes required for viral replication and expression are the N, P, L, and M2-1 genes. However, the Applicant indicates that the M2-1 may not be required. Page 5, lines 19-28. Thus, it is unclear if the M2-1 gene is included as a key domain. Further, the F and G proteins are both the primary antigen proteins of the virus, and are required for viral infectivity. It is therefore assumed, but not clear, that the genes encoding these proteins may also be considered key domains. Because the Applicant has not defined what domains are considered key, the claims are indefinite.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. **(Prior Rejection-Withdrawn)** A prior rejection was maintained over claims 17 and 36-40 in the Final action under 35 U.S.C. 112, first paragraph, because the claims were not enabled for vaccines comprising unattenuated RSV particles. In view of the cancellation of these claims, and the language of the newly added claims requiring the attenuated phenotypes, the rejection is withdrawn.

14. **(New Rejection)** Claims 49-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions, does not reasonably provide enablement for anti-RSV vaccines. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. It will be noted that this rejection is a restatement of a rejection that has previously been withdrawn. Upon further consideration, the rejection is hereby re-instated. The claims read on anti-RSV vaccines comprising attenuated RSV particles with a genetic alteration to a key domain of the viral protein.

In the paper filed on December 5, 2003, the Applicant traversed the original rejection for lack of enablement for RSV vaccines on three grounds. First, the Applicant argued that the application demonstrates that the disclosed virus compositions are effective in the protection of animals against RSV infection, and that it would be routine for those in the art to optimize the dosages and administration routes for human use. December 2002 Response, pages 3-4. Second, on pages 4-5 of that Response, the Applicant argues that they have demonstrated the protective effect of the claimed viruses in animals known as models in the art. Third and last, the Applicant argued that the Examiner had not met the standard for lack of enablement, identified by

Applicant as a demonstration by the Examiner that the claimed invention is "totally incapable of achieving a useful result." These traversals are not found persuasive, and the rejection is therefore reinstated.

The first and second arguments in traversal are related. Each indicates either the Applicant has established the operability of the claimed invention, or that the art has demonstrated the efficacy of the claimed compositions as vaccines against RSV infection. These arguments are based on the assertion that the demonstration that a protective response in animal models are predictive of the results in humans. The Applicant argues that the efficacy of the claimed vaccines in animals has been shown, that Applicant has provided assays by which the protective response of attenuated virus may be determined, and that the use in humans would therefore require only optimization of the techniques used in animals.

However, while the use of accepted models for a disease may be predictive of human responses to a potential therapy for the disease, such is not presently the case with respect to RSV infections. That is, the art does not show an acceptance of a particular animal model as predictive of human responses to RSV vaccines. In specific, while the art is aware of the mouse, cotton rat, and Green monkey models of RSV, those in the art have nonetheless failed to successfully vaccinate against RSV infection. See e.g., Dudas et al., Clin Microbiol Rev 11(3): 430-39, esp. page 432 (indicating that although animal models provide information regarding the potential vaccines, the vaccines so identified have not been established as protective in humans). See also, Prince et al., J Virol 74(22): 10287-92; and, more recently, Tang et al., J Virol 77(20): 10819-28. Each of the Prince and Tang articles indicates that, to date, there are no effective anti-RSV vaccines for humans. Rather, while numerous vaccine candidates have been tested, several

challenges have arisen in the development of such vaccines which have prevented the identification of one that is safe and effective in people. Thus, while the Applicant may have demonstrated that certain embodiments of the claimed composition may be effective in inducing immune responses in animals, the Applicant has not enabled the use of the claimed attenuated virus as a vaccine for humans.

In the Applicant's third argument in traversal, the Applicant asserts that the Federal Circuit has determined that the Federal Circuit indicated that the standard for 112 ¶ 1 lack of enablement is that the invention is "totally incapable of achieving a useful result," and that the Examiner has failed to demonstrate this with respect to the claimed invention. It is noted that the Examiner has not made a utility rejection in the present case. It is further noted that the Applicant's support for their statement regarding the standard for enablement under 112 paragraph 1 in error. The Applicant cites the Federal Circuit decision of Brooktree v Advances Micro Devices (24 U.S.P.Q. 2d 1401, 1412) in support of their assertion. They have, however, misquoted the court. The court actually states "To violate Section 101 the claimed device must be totally incapable of achieving a useful result..." The court clearly indicates that this is the standard for utility rejections under 35 U.S.C. 101, and not for enablement rejections under 35 U.S.C. 112. Thus, the Applicant has misidentified the standard of determining lack of enablement. While the court in that case indicated that the utility standard was relevant to the enablement rejection in that case, the reason was, as indicated by the court, that the same facts were determinative of both rejections. Because the current application is rejected for lack of enablement, and not lack of utility, and because the Applicant has not found to have provided an

enabling disclosure for the full scope of the claims as indicated above, this traversal is not found persuasive, and the rejection is reinstated and maintained.

Claim Rejections - 35 USC § 102

15. **(Prior Rejections-Withdrawn)** Now cancelled claims 17-18, 22-32, and 35-40 were rejected as anticipated by two references 1) Collins et al. (WO 97/12032), and 2) Murphy et al. (U.S. Patent 5,993,824). In view of the cancellation of these claims the rejection is withdrawn.

16. **(New Rejection)** Claims 49, 50, and 52 are rejected under 35 U.S.C. 102(a) as being anticipated by Crowe et al., Vaccine 12(8): 691-99, in light of the teachings of Murphy (U.S. Patent 5,993,824). These claims read on attenuated RSV particles comprising a mutation in the genome, and the reverse complement of a polymerase binding site. For the purposes of this rejection, the term "key" domain is being interpreted as indicating that a gene or domain is important to the virus as a whole. As the L protein of the virus is disclosed in the application as an essential RSV protein (see e.g., page 33, lines 21-24, indicating that the L protein is an essential helper protein in RSV; and page 26, lines 30-31, indicating that the L protein is important to RSV attenuation), the protein is considered a key domain. Thus, the claims read on attenuated RSV particles comprising a mutation in a key domain, including embodiments wherein the virus comprises a mutation in the L protein.

Crowe teaches an attenuated RSV particles designated RSV cpts-248 and RSC cpts-530. These virus are disclosed in column 15, lines 44-64 of U.S. patent 5,993,824 as comprising genetic mutations in the gene coding for the L protein of the RSV virus. Thus, the Crowe reference discloses an attenuated RSV particle with a mutation in a key functional domain- the gene encoding the L protein. The reference therefore anticipates the identified claims.

17. **(New Rejection)** Claims 49-52 are rejected under 35 U.S.C. 102(a) as being anticipated by Crowe et al., Vaccine 12(9): 783-790, in light of the teachings of Murphy (U.S. Patent 5,993,824). The claims have been described in part above. Claim 51 reads on the claims attenuated RSV wherein the virus comprises a mutation in a key regulatory domain. As indicated above, it is not clear what domains of the RSV genome fall within the scope of a "key regulatory domain." However, for the purposes of this rejection, the claims are being interpreted so as to include mutations in the start codon of the RSV M2 gene start sequence.

Crowe discloses an attenuated virus designated RSV cpts-248/404. The Murphy patent discloses in column 4, lines 16-27, that this virus comprises a mutation in the M2 start sequence. Further, the Firestone reference (reference CS in the July 2003 IDS) discloses that this virus comprises mutations not only in the M2 start sequence, but also in the gene encoding the L protein. Firestone, abstract. Thus, although the Crowe reference does not disclose that the virus has such mutations, it is clear from the later teachings in the art that the virus disclosed by Crowe meets the limitations of the rejected claims.

Claim Rejections - 35 USC § 103

18. **(Prior Rejection-Withdrawn)** Claims 17, 18, 22-32, and 35-40 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (PNAS 92:11563-11567) in view of Olmstead et al. (PNAS 83:7462-7466). In view of the cancellation of these claims, the rejection is withdrawn.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
January 12, 2004

James C. Housel 1/12/04

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